Chemical/Biological Terrorism
March-April 2005

1: Acad Emerg Med. 2005 Jan;12(1):45-50.
Online bioterrorism continuing medical education: development and preliminary testing.
Terndrup T, Nafziger S, Weissman N, Casebeer L, Pryor E.
Department of Emergency Medicine, Center for Emergecny Care and Disaster Preparedness, University of Alabama at Birmingham, JTN 266, 619 19th Street, Birmingham, AL 35249-7013, USA. tterndrup@uabmc.edu
OBJECTIVE: Education to achieve awareness and competency in responding to incidents of bioterrorism is important for health care professionals, especially emergency physicians and nurses, who are likely first points of medical contact. The authors describe the development of a computer-based approach to initial education, incorporating a screensaver to promote awareness and a Web-based approach to provide initial content competency in the areas of smallpox and
anthrax. METHODS: Screensavers were developed and tested on emergency department rotating senior medical students and internal medicine interns. Conceptually, screensavers were designed as "billboards" for attracting attention to the educational domain. Five rotating images sequenced at five-second intervals incorporated a teaser question and an interactive toolbar. An interactive toolbar was linked to a Web site that provided content on smallpox and anthrax for hospital-based specialties (emergency physicians and nurses, infection control practitioners, pathologists, and radiologists). The content included both summary and comprehensive content as well as free continuing education credits in an online, specialty-specific, case-scenario format with remediation pop-up boxes. RESULTS: Formal testing indicated that the screensaver and Web site combination deployed on computers in the emergency department and the events of the fall of 2001 significantly increased the percentage of correct responses to five standardized bioterrorism questions. Formal evaluation with a randomized trial and long-term follow-up is ongoing. CONCLUSIONS: Screensavers and Web sites can be used to increase awareness of bioterrorism. Web-based education may provide an effective means of education for bioterrorism.
PMID: 15635137 [PubMed - indexed for MEDLINE]

2: Acta Neurol Scand. 2005 Jan;111(1):1-6.
The role of clinical neurophysiology in bioterrorism.
Prakash KM, Lo YL.
National Neuroscience Institute, Singapore General Hospital Campus, Singapore. gnrpk@sgh.com.sg
Chemical and biological agents have been used as weapons of mass destruction for a long time and presents as a serious threat to mankind. They have been used in many great wars and terrorist attacks with devastating results. The knowledge about these weapons of mass destruction is crucial to health care providers. Early recognition of the clinical characteristics of poisoning as a result of these chemical and biological agents is important to initiate appropriate
therapy and minimizing casualties. Neurophysiological investigations when integrated with clinical features are helpful in early identification of some of these agents, especially when

serological confirmation is not rapidly available. In this review, we have focused on chemical and biological weapons, which affect the nervous system and the role of clinical neurophysiology in such conditions. Blackwell Munksgaard 2004
Publication Types: Review
PMID: 15595931 [PubMed - indexed for MEDLINE]

3: Acta Ophthalmol Scand. 2005 Feb;83(1):26-30.
Trinitrotoluene (TNT)-induced cataract in Danish arms factory workers.
Kruse A, Hertel M, Hindsholm M, Viskum S.
Department of Ophthalmology, Aalborg Hospital, Hobrovej 18-22, PO Box 365, DK-9100 Aalborg, Denmark. lakruse@tdcadsl.dk
PURPOSE: To compare the prevalence of cataract in workers exposed to trinitrotoluene (TNT) to the prevalence in a group of unexposed workers, matched on age and sex, using Tiukina's description and grading of TNT-induced cataract. METHODS: A total of 23 TNT-exposed and 44 unexposed workers underwent an eye examination performed by an ophthalmologist who did not know the exposure status of the subjects. All lens opacities matching Tiukina's description were
classified as TNT cataract and graded on Tiukina's scale of stages 1-4. RESULTS: Four cases of TNT-induced cataract were identified among the 23 TNT-exposed workers and none in the unexposed group ($p < 0.01$). CONCLUSION: Exposure to TNT may cause a unique type of cataract, which a general ophthalmologist, using Tiukina's description and grading scale, will be able to distinguish from other cataracts.
PMID: 15715553 [PubMed - indexed for MEDLINE]

4: Am J Health Syst Pharm. 2005 Feb 1;62(3):239-40.
Nation is unprepared for bioterrorism threat, study finds.
Young D.
Publication Types: News
PMID: 15719576 [PubMed - in process]

5: Am J Ind Med. 2004 Nov;46(5):432-45.
Hospital response to chemical terrorism: personal protective equipment, training, and operations planning.
Georgopoulos PG, Fedele P, Shade P, Lioy PJ, Hodgson M, Longmire A, Sands M, Brown MA.
Environmental and Occupational Health Sciences Institute (EOHSI), UMDNJ-RW Johnson Medical School and Rutgers University, 170 Frelinghuysen Road, Piscataway, NJ 08854, USA. panosg@ccl.rutgers.edu
BACKGROUND: Hospitals distant from the immediate site of an incident involving a hazardous materials (HAZMATs) release which could include chemical warfare agents, must develop emergency response plans (ERPs) to protect healthcare professionals if they receive potentially contaminated victims. The ERP must address OSHA, EPA, and JCAHO requirements. METHODS: The VHA convened groups to develop a hazard and exposure assessment, identify actions for compliance with existing regulatory standards, and review site and operational planning issues. Exposure modeling results were used to derive relationships between operational parameters (time and distance from sites/sources) and potential exposure for healthcare workers. RESULTS: According to exposure modeling, level C personal protective equipment is adequate to protect hospital staff distant from the chemical release site. Decontamination runoff and contaminated clothing should also be controlled to limit exposure. CONCLUSIONS: Development and coordination of ERPs must include the local emergency planning committee, with clear assignment of tasks, locations, and training in order to prevent exposures to healthcare workers. Copyright 2004 Wiley-Liss, Inc.
PMID: 15490471 [PubMed - indexed for MEDLINE]

6: Am J Orthopsychiatry. 2002 Oct;72(4):486-91.
Preparing for bioterrorism at the state level: report of an informal survey.
Hall MJ, Norwood AE, Fullerton CS, Ursano RJ.
Department of Psychiatry, Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814, USA.

Members of 18 states' departments of mental health were interviewed about their plans for managing the psychosocial impacts of a bioterrorism event. Questions were developed from recommendations of an international conference on planning for bioterrorism ("Planning for bioterrorism," 2000). Information derived from the survey highlights the need for, and the importance of, mental health consultation to the state's planning process. Familiarity with the unique psychological and behavioral consequences of a bioterrorism event in contrast to natural disasters is essential. Realistic training scenarios that incorporate likely psychosocial impacts and appropriate mental health response must be developed.
PMID: 15792034 [PubMed - in process]

7: Am J Public Health. 2005 Mar;95(3):489-95.
In their own words: lessons learned from those exposed to anthrax.
Blanchard JC, Haywood Y, Stein BD, Tanielian TL, Stoto M, Lurie N.
George Washington University Department of Emergency Medicine, 2150 Pennsylvania Ave, NW, Washington, DC, 20037, USA. jblanchard@mfa.gwu.edu
OBJECTIVES: We evaluated perceptions of workers at the US Postal Service Brentwood Processing and Distribution Center and US Senate employees regarding public health responses to the anthrax mailings of October 2001. We generated recommendations for improving responses to bioterrorism on the basis of the perceptions we recorded. METHODS: Transcripts from focus groups conducted with Brentwood and US Senate employees were examined, and qualitative analysis identified common domains. RESULTS: Brentwood focus groups consisted of 36 participants (97% African American and 19% hearing impaired). US Senate focus groups consisted of 7 participants (71% White and 0% hearing impaired). The focus groups revealed that participants' trust in public health agencies had eroded and that this erosion could threaten the effectiveness of communication during future public health emergencies. Among Brentwood participants, lack of trust involved the perception that unfair treatment on the basis of
race/ethnicity and socioeconomic status had occurred; among US Senate participants, it derived from perceptions of inconsistent and disorganized messages. CONCLUSIONS: Effective communication during a public health emergency depends on the provision of clear messages and close involvement of the affected community. Diverse populations may require individualized approaches to ensure that messages are delivered appropriately. Special attention should be given to those who face barriers to traditional modes of communication.
PMID: 15727982 [PubMed - indexed for MEDLINE]

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Comment on: Am J Public Health. 2004 Oct;94(10):1667-71.
Bioterrorism preparedness funds well used at the local level.
Amadio JB.
Publication Types: Comment Review Review, Tutorial
PMID: 15727958 [PubMed - indexed for MEDLINE]

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Comment on: Am J Public Health. 2004 Oct;94(10):1667-71.
Bioterrorism preparedness: potential threats remain.
Rumm PD.
Publication Types: Comment Letter Review Review, Tutorial
PMID: 15727957 [PubMed - indexed for MEDLINE]

10: Annu Rev Public Health. 2005;26:213-37.
WATER AND BIOTERRORISM: Preparing for the Potential Threat to U.S. Water Supplies and Public Health.
Meinhardt PL.
Center for Occupational and Environmental Medicine, Arnot Ogden Medical Center, Elmira, New York 14905; email: pmeinhardt@aomc.org.
Water supplies and water distribution systems represent potential targets for terrorist activity in the United States because of the critical need for water in every sector of our industrialized society. Even short-term disruption of water service can significantly impact a community, and

intentional contamination of a municipal water system as part of a terrorist attack could lead to serious medical, public health, and economic consequences. Most practicing physicians and public health professionals in the United States have received limited training in the recognition and evaluation of waterborne disease from either natural or intentional contamination of water. Therefore, they are poorly prepared to detect water-related disease resulting from
intentional contamination and may not be adequately trained to respond appropriately to a terrorist assault on water. The purpose of this review is to address this critical information gap and present relevant epidemiologic and clinical information for public health and medical practitioners who may be faced with addressing the recognition, management, and prevention of water terrorism in their communities.
PMID: 15760287 [PubMed - in process]

11: Appl Environ Microbiol. 2005 Jan;71(1):566-8.
Chlorine inactivation of bacterial bioterrorism agents.
Rose LJ, Rice EW, Jensen B, Murga R, Peterson A, Donlan RM, Arduino MJ.
Centers for Disease Control and Prevention, 1600 Clifton Rd., C16, Atlanta, GA 30333, USA. lrose@cdc.gov
Seven species of bacterial select agents were tested for susceptibility to free available chlorine (FAC). Under test conditions, the FAC routinely maintained in potable water would be sufficient to reduce six species by 2 orders of magnitude within 10 min. Water contaminated with spores of Bacillus anthracis spores would require further treatment.
PMID: 15640238 [PubMed - indexed for MEDLINE]

12: Arch Toxicol. 2004 Sep;78(9):508-24. Epub 2004 May 29.
Retrospective detection of exposure to nerve agents: analysis of phosphofluoridates originating from fluoride-induced reactivation of phosphylated BuChE.
van der Schans MJ, Polhuijs M, van Dijk C, Degenhardt CE, Pleijsier K, Langenberg JP, Benschop HP.
Department of Medical Countermeasures, TNO Prins Maurits Laboratory, P.O. Box 45, 2280 AA Rijswijk, The Netherlands. schansm@pml.tno.nl
The utility was explored of a new approach to detect retrospectively exposure to nerve agents by means of conversion of the inhibitor moiety bound to the active site of the enzyme BuChE in plasma with fluoride ions into a phosphofluoridate which is subsequently analyzed by means of gas chromatography (GC). This quantifies >or=0.01% inhibition of BuChE and identifies the structure of the inhibitor except for the original leaving group. A three-tiered approach was followed involving the five classical nerve agents GA, GB, GF, GD, and VX, as well as the active metabolite of parathion, i.e., paraoxon: in vivo experiments in rhesus monkeys after iv administration of a sign-free dose of agent and concomitant in vitro experiments in plasma of rhesus monkeys and humans should allow an assessment of in vivo retrospectivity in humans. A systematic investigation was performed in order to find a single set of reaction conditions which yields a maximum amount of phosphofluoridate for all nerve agents. Fluoride-induced reactivation at 25 degrees C at a final concentration of 250 mM KF during 15 min in a pH-range between 4 and 6 appears to be effective. The in vitro decrease with time in reactivatibility of inhibited BuChE in plasma from humans and rhesus monkeys was largely due to aging of the phosphyl moiety, except for VX where spontaneous reactivation was a major cause. The decrease followed first-order except for a biphasic course in the case of GF in human and
rhesus monkey plasma as well as of GD in rhesus plasma. In vitro half-lifes in human plasma ranged between ca. 14 h for GB and ca. 63 h for GA. A comparison of the in vivo data from rhesus monkeys and the in vitro data is complicated by the observation that the in vivo decrease with time of fluoride-reactivated phosphofluoridate is biphasic for all nerve agents. The terminal in vivo phase pertains to a small fraction of the amount of initially regenerated phosphofluoridate but is responsible for a considerable degree of retrospectivity, ranging between 14 and 56 days for GF and GB, respectively. The new procedure can be used in a variety of practical applications, e.g., (i) biomonitoring in health surveillance at exposure levels that are several orders of magnitude lower than presently possible; (ii) diagnosis in case of alleged exposure to nerve agents in time of war or after terrorist attacks; (iii) in forensic

cases against suspected terrorists that have handled organophosphate anticholinesterases; and (iv) in research applications such as investigations on lowest observable effect levels of exposure to nerve agents.
PMID: 15170525 [PubMed - indexed for MEDLINE]

13: Biosecur Bioterror. 2004;2(4):328-41.
Executive government positions of influence in biodefense: the Bio-Plum book.
Schuler A, Fitzgerald J, Inglesby TV, O'Toole T.
Center for Biosecurity of the University of Pittsburgh Medical Center, Baltimore, Maryland 21202, USA. aschuler@upmc-biosecurity.org
PMID: 15650442 [PubMed - indexed for MEDLINE]

14: Biosecur Bioterror. 2004;2(4):320-7.
Taking the measure of countermeasures: leaders' views on the nation's capacity to develop biodefense countermeasures.
Gilfillan L, Smith BT, Inglesby TV, Kodukula K, Schuler A, Lister M, O'Toole T.
Government Operations, Sarnoff Corporation, Arlington, VA 22209, USA. lgilfillan@sarnoff.com
PMID: 15650441 [PubMed - indexed for MEDLINE]

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Challenges in managing volunteers during bioterrorism response.
Clizbe JA.
Health Department, Alexandria, Virginia 22314, USA. John.clizbe@verizon.net
PMID: 15650439 [PubMed - indexed for MEDLINE]

16: Biosecur Bioterror. 2004;2(4):281-93.
Risk of occupationally acquired illnesses from biological threat agents in unvaccinated laboratory workers.
Rusnak JM, Kortepeter MG, Hawley RJ, Anderson AO, Boudreau E, Eitzen E.
Special Immunizations Clinic, U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, Maryland 21702, USA. Janice.Rusnak@det.amedd.army.mil
Many vaccines for bioterrorism agents are investigational and therefore not available (outside of research protocol use) to all at-risk laboratory workers who have begun working with these agents as a result of increased interest in biodefense research. Illness surveillance data archived from the U.S. offensive biological warfare program (from 1943 to 1969) were reviewed to assess the impact of safety measures on disease prevention (including biosafety cabinets
[BSCs]) before and after vaccine availability. Most laboratory-acquired infections from agents with higher infective doses (e.g., anthrax, glanders, and plague) were prevented with personal protective measures and safety training alone. Safety measures (including BSCs) without vaccination failed to sufficiently prevent illness from agents with lower infective doses in this high-risk research setting. Infections continued with tularemia (average 15/year), Venezuelan equine encephalitis (1.9/year), and Q fever (3.4/year) but decreased dramatically once vaccinations became available (average of 1, 0.6, and 0 infections per year, respectively). While laboratory-acquired infections are not expected to occur frequently in the current lower-risk biodefense research setting because of further improvements in biosafety equipment and changes in biosafety policies, the data help to define the inherent risks of working with the specific agents of bioterrorism. The data support the idea that research with these agents should be restricted to laboratories with experience in handling highly hazardous agents and where appropriate safety training and precautions can be implemented.
PMID: 15650438 [PubMed - indexed for MEDLINE]

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Agroterrorism: betting far more than the farm.
Breeze R.
Centaur Science Group, Washington, DC 20007, USA. breezerg@centaurscience.com
PMID: 15650435 [PubMed - indexed for MEDLINE]

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Interview with Marcelle C. Layton, MD assistant commissioner, Bureau of Communicable Disease New York City Department of Health and Mental Hygiene. Interview by Madeline Drexler.
Layton MC.
Publication Types: Interview
PMID: 15650434 [PubMed - indexed for MEDLINE]

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Bacteria as potential tools in bioterrorism, with an emphasis on bacterial toxins.
Clarke SC.
Scottish Meningococcus and Pneumococcus Reference Laboratory, Glasgow, UK. stuartcclarke@hotmail.com
The threat of bioterrorism remains a reality worldwide and, although of low probability, an attack would be a high-consequence event. Microbes are available to individuals with appropriate contacts and even many low-grade bacterial pathogens can severely affect health. Toxins provide bacteria with a system of defence that is often detrimental to humans and their versatility makes them potential tools of bioterrorism. It should be remembered that the aim of terrorism is not always to kill but rather to strike fear into peoples lives. Therefore, agents such as botulinum and cholera toxin could be used, which may not cause significant mortality but would cause widespread panic and potentially high morbidity. Importantly, no state can ever be fully prepared for a response and it is probable that no state ever could be. It is for this reason that biological agents are so attractive as weapons.
PMID: 15816214 [PubMed - in process]

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Bioterrorism, public health, and international law.
Fidler DP.
Indiana University School of Law-Bloomington, USA.
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Canada: Soldiers have right to refuse anthrax vaccine.
Walker R.
Publication Types: Newspaper Article
PMID: 15586926 [PubMed - indexed for MEDLINE]

22: Clin Immunol. 2005 Mar;114(3):227-38.
Cellular bioterrorism: how Brucella corrupts macrophage physiology to promote invasion and proliferation.
Maria-Pilar Jde B, Dudal S, Dornand J, Gross A.
Unidad de Sanidad Animal, Servicio de Investigacion Agroalimentaria, Diputacion General de Aragon, Ap. 727. 50080 Zaragoza, Spain.
Brucellosis is a worldwide human zoonosis caused by intracellular bacteria of the genus Brucella. Virulence factors play an important role in allowing Brucella infection and proliferation within macrophages. Brucella enters macrophages through lipid raft microdomains, avoids phagolysosome fusion, and inhibits TNF-alpha secretion and apoptosis. Furthermore, Brucella can perturb bactericidal activity in macrophages by influencing the host cell response to its advantage through its LPS or by activating the cAMP/PKA pathway. To date, small steps have been taken in defining and understanding the virulence factors of Brucella used in macrophage subversion, but further investigation is required to fully explain virulence and persistence.
PMID: 15721833 [PubMed - in process]

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Sulfur mustard: cutaneous exposure.
Carroll LS.

Department of Emergency Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA. carrolls@tuhs.temple.edu
Publication Types: Case Reports
PMID: 15732448 [PubMed - indexed for MEDLINE]

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Bioterrorism: Preparing for the impossible or the improbable.
Karwa M, Currie B, Kvetan V.
Division of Critical Care Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA. mkarva@montefiore.org
OBJECTIVE: To review the current literature surrounding the history of bioterrorism, the relative risk of a bioterrorist attack, methods of surveillance for biological agents, identification and management of various biological agent casualties, as well as the role of the intensivist in managing a bioterrorist attack. METHODS: Internet and Medline search (from 1966 to 2004) for articles relating to bioterrorism, biological agents, biological warfare, hospital preparedness, disaster management, and intensive care. CONCLUSIONS: There are few instances of a successful large-scale biological weapons attack in history. Weaponization of biological agents for aerosol dispersal is difficult and has often proved to be the rate-limiting step for a successful attack. Although a successful biological attack is currently unlikely, it is still feasible. More importantly, the threat of one is likely to cause much panic in the public, while a successful attack would overburden the current healthcare infrastructure. Intensivists will need to have specific knowledge of identifying and managing casualties from various biological agents. In addition, they will need to play an integral part in the preparedness of their institutions and communities for managing a bioterrorist event.
Publication Types: Historical Article Review Review, Tutorial
PMID: 15640684 [PubMed - indexed for MEDLINE]

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Critical care requirements after mass toxic agent release.
Baker DJ.
Department of Anaesthesia and Critical Care, Hopital Necker-Enfants Malades, Paris, France.
There is an increasing risk of mass exposure of civil populations after release of toxic agents. These include military chemical warfare agents or industrial compounds, some of which have been used as a chemical. The traditional military divisions among chemical agents, toxins, and biologic agents may be viewed as a continuous spectrum of hazards. Each of these has four specific qualities (toxicity, latency, persistency, and transmissibility), which determine management of casualties and the toxic release. Toxic hazards may be released accidentally or deliberately, producing potentially large numbers of casualties. Previous incidents have shown that many of these require extended hospital care. This article reviews aspects of the nature of the toxic agents, the pathophysiology they produce, and therapeutic measures. The central and
peripheral nervous systems and the respiratory systems are particularly vulnerable and may lead to fatal results unless early action is taken. Specific antidotes and life support care is required at all levels of prehospital and hospital management. Critical care management is required for severe cases, and this must combine continuing antidote, ventilatory and supportive therapy.
Publication Types: Review Review, Tutorial
PMID: 15640682 [PubMed - indexed for MEDLINE]

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Keeping up with bioterrorism fears.
Gross M.
Publication Types: News
PMID: 15530373 [PubMed - indexed for MEDLINE]

27: Emerg Infect Dis. 2005 Jan;11(1):69-76.
HEPA/vaccine plan for indoor anthrax remediation.
Wein LM.

Stanford University, Stanford, California, USA.
We developed a mathematical model to compare 2 indoor remediation strategies in the aftermath of an outdoor release of 1.5 kg of anthrax spores in lower Manhattan. The 2 strategies are the fumigation approach used after the 2001 postal anthrax attack and a HEPA/vaccine plan, which relies on HEPA vacuuming, HEPA air cleaners, and vaccination of reoccupants. The HEPA/vaccine approach leads to few anthrax cases among reoccupants if applied to all but the most heavily contaminated buildings, and recovery is much faster than under the decades-long fumigation plan. Only modest environmental sampling is needed. A surge capacity of 10,000 to 20,000 Hazmat workers is required to perform remediation within 6 to 12 months and to avoid permanent mass relocation. Because of the possibility of a campaign of terrorist attacks, serious
consideration should be given to allowing or encouraging voluntary self-service cleaning of lightly contaminated rooms by age-appropriate, vaccinated, partially protected (through masks or hoods) reoccupants or owners.
PMID: 15705325 [PubMed - indexed for MEDLINE]

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Demand for prophylaxis after bioterrorism-related anthrax cases, 2001.
Belongia EA, Kieke B, Lynfield R, Davis JP, Besser RE.
Epidemiology Research Center (ML2), Marshfield Clinic Research Foundation, 1000 North Oak Avenue, Marshfield, WI 54449, USA. belongia.edward@mcrf.mfldclin.edu
Media reports suggested increased public demand for anthrax prophylaxis after the intentional anthrax cases in 2001, but the magnitude of anthrax-related prescribing in unaffected regions was not assessed. We surveyed a random sample of 400 primary care clinicians in Minnesota and Wisconsin to assess requests for and provision of anthrax-related antimicrobial agents. The survey was returned by 239 (60%) of clinicians, including 210 in outpatient practice. Fifty-eight
(28%) of those in outpatient practice received requests for anthrax-related antimicrobial agents, and 9 (4%) dispensed them. Outpatient fluoroquinolone use in both states was also analyzed with regression models to compare predicted and actual use in October and November 2001. Fluoroquinolone use as a proportion of total antimicrobial use was not elevated, and anthrax concerns accounted for an estimated 0.3% of all fluoroquinolone prescriptions. Most physicians in
Minnesota and Wisconsin managed anthrax-related requests without dispensing antimicrobial agents.
PMID: 15705321 [PubMed - indexed for MEDLINE]

29: Emerg Med J. 2004 Jan;21(1):84-8.
Prehospital management and medical intervention after a chemical attack.
Kenar L, Karayilanoglu T.
Department of NBC Defence, Gulhane Military Medical Academy, Ankara, Turkey. lkenar@gata.edu.tr
Chemical warfare agents are toxic weapons and emergency prehospital medical care providers should be well prepared, trained, and equipped to give response. Personnel need to be aware of the following medical issues regarding prehospital management of a chemical attack, event recognition, incident medical command and control, safety and protection, decontamination, isolation of the incident area (hot zone, warm zone, and cold zone), sampling and detection, psychological management, communication, triage, treatment, transportation, recovery activities and fatality management. During prehospital response, healthcare responders should provide self protection by wearing proper protective equipment and ensuring that the casualty is thoroughly decontaminated. Medical first responders are also responsible for performing triage in each zone of the incident area. Victims are triaged into four categories based on the need for medical care; immediate, delayed, minimal, and expectant. Finally, a medical emergency planning should be completed, and exercises conducted to test the system before an event occurs.
PMID: 14734392 [PubMed - indexed for MEDLINE]

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Emergency department response to the deliberate release of biological agents.
Ollerton JE.
Department of Trauma, Liverpool Hospital, Sydney, NSW 1871, Australia.
j.ollerton@doctors.org.uk
Bioterrorism is the use of biological agents outside the arena of war. Its purpose is to disrupt civilian life. This article investigates the role of the emergency department in the event of an act of bioterrorism.
Publication Types: Review Review, Tutorial
PMID: 14734365 [PubMed - indexed for MEDLINE]

31: Emerg Med Serv. 2004 Aug;33(8):99-104.
Under attack! Protecting EMS personnel.
Hanson D.
dougmh@comcast.net
PMID: 15368984 [PubMed - indexed for MEDLINE]

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Theoretical perspectives on public communication preparedness for terrorist attacks.
Wray RJ, Kreuter MW, Jacobsen H, Clements B, Evans RG.
Health Communication Research Laboratory, School of Public Health, Saint Louis University, 3545 Lafayette Avenue, St. Louis, MO 63104, USA. wray@slu.edu
The experience of federal health authorities in responding to the mailed anthrax attacks in the Fall of 2001 sheds light on the challenges of public information dissemination in emergencies. Lessons learned from the Fall of 2001 have guided more recent efforts related to crisis communication and preparedness goals. This article applies theories and evidence from the field of communication to provide an orientation to how public health communication can best contribute to the preparedness effort. This theoretical orientation provides a framework to systematically assess current recommendations for preparedness communication.
PMID: 15596970 [PubMed - indexed for MEDLINE]

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Project Bioshield: protecting Americans from terrorism.
Meadows M.
PMID: 15675025 [PubMed - indexed for MEDLINE]

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Possession, use, and transfer of select agents and toxins. Final rule.
Centers for Disease Control and Prevention, Office of Inspector General, Department of Health and Human Services (HHS).
This document establishes a final rule regarding possession, use, and transfer of select agents and toxins. The final rule implements provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and is designed to protect public health and safety. In a companion document published in this issue of the Federal Register, the United States Department of Agriculture has established corresponding final rules designed to protect animal and plant health and animal and plant products.
PMID: 15776528 [PubMed - indexed for MEDLINE]

35: Gen Hosp Psychiatry. 2004 Sep-Oct;26(5):359-66.
Hospital preparedness for possible nonconventional casualties: an Israeli experience.
Schreiber S, Yoeli N, Paz G, Barbash GI, Varssano D, Fertel N, Hassner A, Drory M, Halpern P.
Department of Psychiatry, Tel Aviv Sourasky Medical Center, Weizmann Street 6, Tel Aviv, Israel. shaulsch@tasmc.health.gov.il
Since 9/11, hospitals and health authorities have been preparing medical response in case of various mass terror attacks. The experience of Tel Aviv Sourasky Medical Center in treating suicide-bombing mass casualties served, in the time leading up to the war in Iraq, as a platform for launching a preparedness program for possible attacks with biological and chemical agents of

mass destruction. Adapting Quarantelli's criteria on disaster mitigation to the "microinfrastructure" of the hospital, and including human behavior experts, we attempted to foster an interactive emergency management process that would deal with contingencies stemming from the potential hazards of chemical and biological (CB) weapons. The main objective of our work was to encourage an organization-wide communication network that could effectively address the
contingent hazards unique to this unprecedented situation. A stratified assessment of needs, identification of unique dangers to first responders, and assignment of team-training sessions paved the way for program development. Empowerment through leadership and resilience training was introduced to emergency team leaders of all disciplines. Focal subject matters included proactive planning, problem-solving, informal horizontal and vertical communication, and coping through stress-management techniques. The outcome of this process was manifested in an "operation and people" orientation supporting a more effective and compatible emergency management. The aim of article is to describe this process and to point toward the need for a broad-spectrum view in such circumstances. Unlike military units, the civilian hospital staff at risk,
expected to deal with CB casualties, requires adequate personal consideration to enable effective functioning. Issues remain to be addressed in the future. We believe that collaboration and sharing of knowledge, information, and expertise beyond the medical realm is imperative in assisting hospitals to expedite appropriate preparedness programs.
PMID: 15474635 [PubMed - indexed for MEDLINE]

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Baldwin FD.
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Disaster readiness. Keeping safe.
Meyers S.
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Administrative issues related to infectious disease research in the age of bioterrorism.
Jaax J.
Research Compliance, Kansas State University, Manhattan, Kansas, USA.
The recent unprecedented growth in infectious disease research funding and infrastructure has resulted in part from an outgrowth of concern about newly emerging and re-emerging diseases and the progressive development of antibiotic-resistant pathogens. However, the most compelling impetus is the suspected and demonstrated capability and will of unknown individuals, groups,
or states to use biological agents and/or toxins as weapons. Although the actual number of known victims and fatalities from bioterrorism in the United States has been miniscule compared with many other daily hazards, biological agents have the potential to cause human mass casualties, severely damage segments of our economy or agricultural infrastructure, poison or compromise our food or water supply, and, perhaps most damaging, disrupt our society physically and psychologically. The significant institutional commitment necessary to participate in infectious disease research is described, with a focus on programs that involve research with pathogens thought to have potential for use by bioterrorists. Administrative considerations are described, and include obtaining necessary research funding to offset high operating costs; complying with "select agent" regulations, security screening of employees; building or renovating a biocontainment facility; finding skilled professional and technical manpower; providing adequate physical security in a threat environment; conducting targeted training; overcoming potential internal and external dissent; developing and/or providing sufficient occupational health and safety programs; achieving and maintaining compliance standards in a fluid regulatory environment; mitigating potentially hazardous working conditions; understanding

personal and institutional liability; and reassuring and dealing with a concerned, skeptical, or even hostile public.
Publication Types: Review Review, Tutorial
PMID: 15644559 [PubMed - indexed for MEDLINE]

39: ILAR J. 2005;46(1):1-3.
Hidden costs of biodefense research.
Barthold SW.
Department of Comparative Medicine, University of California, Davis, USA.
Publication Types: Review Review, Tutorial
PMID: 15644557 [PubMed - indexed for MEDLINE]

40: Indoor Air. 2005 Apr;15(2):127-34.
The effectiveness of stand alone air cleaners for shelter-in-place.
Ward M, Siegel JA, Corsi RL.
Center for Energy and Environmental Resources, Department of Civil Engineering, The University of Texas at Austin, Austin, TX 78758, USA.
Stand-alone air cleaners may be efficient for rapid removal of indoor fine particles and have potential use for shelter-in-place (SIP) strategies following acts of bioterrorism. A screening model was employed to ascertain the potential significance of size-resolved particle (0.1-2 microm) removal using portable high efficiency particle arresting (HEPA) air cleaners in residential buildings following an outdoor release of particles. The number of stand-alone air cleaners, air exchange rate, volumetric flow rate through the heating, ventilating and air-conditioning (HVAC) system, and size-resolved particle removal efficiency in the HVAC filter were varied. The effectiveness of air cleaners for SIP was evaluated in terms of the outdoor and the indoor particle concentration with air cleaner(s) relative to the indoor concentration without
air cleaners. Through transient and steady-state analysis of the model it was determined that one to three portable HEPA air cleaners can be effective for SIP following outdoor bioaerosol releases, with maximum reductions in particle concentrations as high as 90% relative to conditions in which an air cleaner is not employed. The relative effectiveness of HEPA air cleaners vs. other removal mechanisms was predicted to decrease with increasing particle size, because of increasing competition by particle deposition with indoor surfaces and removal
to HVAC filters. However, the effect of particle size was relatively small for most scenarios considered here. PRACTICAL IMPLICATIONS: The results of a screening analysis suggest that stand-alone (portable) air cleaners that contain high efficiency particle arresting (HEPA) filters can be effective for reducing indoor fine particle concentrations in residential dwellings during outdoor
releases of biological warfare agents. The relative effectiveness of stand-alone air cleaners for reducing occupants' exposure to particles of outdoor origin depends on several factors, including the type of heating, ventilating and air-conditioning (HVAC) filter, HVAC operation, building air exchange rate, particle size, and duration of elevated outdoor particle concentration. Maximum particle reductions, relative to no stand-alone air cleaners, of 90% are predicted when three stand-alone air cleaners are employed.
Publication Types: Evaluation Studies
PMID: 15737155 [PubMed - indexed for MEDLINE]

41: Int Immunopharmacol. 2004 Nov;4(12):1455-66.
An in vitro investigation of the effects of the nerve agent pretreatment pyridostigmine bromide on human peripheral blood T-cell function.
Telford G, Wilkinson LJ, Hooi DS, Worrall V, Green AC, Cook DL, Pritchard DI, Griffiths GD.
Immune Modulation Research Laboratory, School of Pharmaceutical Sciences, University of Nottingham, The Boots Science Building, NG7 2RD, UK.
The current pretreatment against nerve agent poisoning deployed by the UK and US armed forces is the acetylcholinesterase (EC 3.1.1.7) inhibitor pyridostigmine bromide (PB). At higher doses, PB is also used to treat the autoimmune disease myasthenia gravis. In both cases, the therapeutic effect is mediated by inhibition of acetylcholinesterase (AChE) at cholinergic

synapses. However, the location of AChE is not restricted to these sites. AChE, acetylcholine (ACh) receptors and choline acetyltransferase have been reported to be expressed by T cells, suggesting that cholinergic signalling may exert some modulatory influence on T-cell function and consequently on the immune system. The aim of this study was to investigate the role of the T-cell cholinergic system in the immunological activation process and to examine whether inhibitors of AChE such as PB affect immune function. To investigate this, human peripheral blood mononuclear cells (PBMC) were stimulated using either mitogen, cross-linking of the T-cell receptor and co-receptors with antibodies (anti-CD3/CD28) or by antigen presentation in the presence of various AChE inhibitors and ACh receptor agonists or antagonist. Several indices were used to assess T-cell activation, including the secretion of IL-2, cell proliferation and expression of CD69. Treatment with PB had no significant effect on the immunological assays
selected. Physostigmine (PHY), a carbamate compound similar to PB, consistently showed inhibition of T-cell activation, but only at concentrations in excess of those required to inhibit AChE. No evidence was found to support previously published findings showing muscarinic enhancement of cell proliferation or IL-2 secretion.
PMID: 15351315 [PubMed - indexed for MEDLINE]

42: Int J Environ Health Res. 2004 Dec;14(6):461-4; author reply 465-9.
Comment on: Int J Environ Health Res. 2004 Feb;14(1):31-41.
How clean is clean enough? Recent developments in response to threats posed by chemical and biological warfare agents,.
Watson A, Opresko D, Young R.
Publication Types: Comment Letter
PMID: 15545041 [PubMed - indexed for MEDLINE]

43: J Am Acad Dermatol. 2004 Sep;51(3):452-3.
Threats of biological and chemical warfare on civilian populations.
Heymann WR.
Publication Types: Review Review, Tutorial
PMID: 15337990 [PubMed - indexed for MEDLINE]

44: J Am Coll Surg. 2005 Feb;200(2):291-302.
The surgeon and acts of civilian terrorism: biologic agents.
Fry DE, Schecter WP, Parker JS, Quebbeman EJ; Governors' Committee on Blood Borne Infection and Environmental Risk of the American College of Surgeons.
University of New Mexico School of Medicine, Albuquerque, NM 87131, USA.
PMID: 15664107 [PubMed - indexed for MEDLINE]

45: J Am Coll Surg. 2005 Jan;200(1):128-35.
The surgeon and acts of civilian terrorism: chemical agents.
Schecter WP, Fry DE; Governors' Committee on Blood Borne Infection and Environmental Risk of the American College of Surgeons.
Department of Surgery, University of California-San Francisco, and SF General Hospital, 10012 Potrero Avenue, San Francisco, CA 94110, USA.
Publication Types: Review Review, Tutorial
PMID: 15631931 [PubMed - indexed for MEDLINE]

46: J Anal Toxicol. 2004 Jul-Aug;28(5):305.
Biological monitoring of human exposure to chemical warfare agents.
Barr JR.
Publication Types: Editorial
PMID: 15307221 [PubMed - indexed for MEDLINE]

47: J Anal Toxicol. 2004 Jul-Aug;28(5):390-2.
Analysis of the enantiomers of VX using normal-phase chiral liquid chromatography with atmospheric pressure chemical ionization-mass spectrometry.
Smith JR.

U.S. Army Medical Research Institute of Chemical Defense, MCMR-UV-PA, 3100 Ricketts Point Road, Aberdeen Proving Ground, Maryland 21010-5400, USA.
john.richard.smith@us.army.mil
The chemical warfare nerve agent O-ethyl S-(2-diisopropylaminoethyl) methylphosphonothioate (VX) is a mixture of two enantiomers resulting from the chiral center at the phosphorus atom. Significant differences exist in the reported toxicity and acetylcholinesterase inhibition rates of the two enantiomers. This makes the ability to distinguish between them desirable for either toxicological studies or the development of antidotal therapies. Using a Chiralcel OD-H column with normal-phase liquid chromatography, the enantiomers were baseline resolved in less than 7 min. Atmospheric pressure chemical ionization was utilized as the interface between a liquid chromatograph and mass spectrometer. The mass spectra of the two enantiomers were virtually identical. The protonated molecule was readily observed at m/z 268. VX was incubated with human plasma for 13 min, followed by hexane extraction. The areas of the first and second eluting VX enantiomers decreased by approximately 40% and 6%, respectively, when compared with VX-spiked plasma samples that were not allowed an incubation phase. Currently, research by others has been directed towards the identification, isolation, and possible modification of enzymes capable of hydrolyzing VX. The method presented here provides an analytical tool capable of monitoring the stereospecificity of enzymes that react with VX.
PMID: 15239861 [PubMed - indexed for MEDLINE]

48: J Anal Toxicol. 2004 Jul-Aug;28(5):372-8.
Quantitation of metabolites of the nerve agents sarin, soman, cyclohexylsarin, VX, and Russian VX in human urine using isotope-dilution gas chromatography-tandem mass spectrometry.
Barr JR, Driskell WJ, Aston LS, Martinez RA.
Centers for Disease Control and Prevention, National Center for Environmental Health, 4770 Buford Highway NE, Mailstop F-47, Atlanta, Georgia 30341, USA.
JBarr@cdc.gov
Organophosphorus nerve agents are among the most toxic organic compounds known and continue to be a threat for both military and terrorist use. We have developed an isotope-dilution gas chromatography-tandem mass spectrometric (GC-MS-MS) method for quantitating the urinary metabolites of the organophosphorus nerve agents sarin (GB), soman (GD), VX, Russian VX (RVX), and cyclohexylsarin (GF). Urine samples were acidified, extracted into ether-acetonitrile, derivatized by methylation with diazomethane, and analyzed by GC-MS-MS. The limits of detection were less than 1 micro g/L for all analytes.
PMID: 15239858 [PubMed - indexed for MEDLINE]

49: J Anal Toxicol. 2004 Jul-Aug;28(5):364-71.
Improvements of the fluoride reactivation method for the verification of nerve agent exposure.
Degenhardt CE, Pleijsier K, van der Schans MJ, Langenberg JP, Preston KE, Solano MI, Maggio VL, Barr JR. TNO-Prins Maurits Laboratory, P.O. Box 45, 2280 AA Rijswijk, The Netherlands.
One of the most appropriate biomarkers for the verification of organophosphorus nerve agent exposure is the conjugate of the nerve agent to butyrylcholinesterase (BuChE). The phosphyl moiety of the nerve agent can be released from the BuChE enzyme by incubation with fluoride ions, after which the resulting organophosphonofluoridate can be analyzed with gas chromatography-mass spectrometry (GC-MS). This paper describes recent improvements of the fluoride-induced reactivation in human plasma or serum samples by enhancing the sample preparation with new solid-phase extraction cartridges and the MS analysis with large volume injections. Analysis is performed with thermal desorption GC with either mass selective detection with ammonia chemical ionization or high-resolution MS with electron impact ionization. The
organophosphorus chemical warfare agents analyzed in this study are O-ethyl S-2-diisopropylaminoethyl methylphosphonothiolate, ethyl methylphosphonofluoridate, isopropyl methylphosphonofluoridate (sarin, GB), O-ethyl N,N-dimethylphosphoramidocyanidate, ethyl

N,N-dimethylphosphoramidofluoridate, and cyclohexyl methylphosphonfluoridate. Detection limits of approximately 10 pg/mL plasma were achieved for all analytes, which corresponds to 0.09% inhibition with GB on a sample with normal BuChE levels.
PMID: 15239857 [PubMed - indexed for MEDLINE]

50: J Anal Toxicol. 2004 Jul-Aug;28(5):357-63.
Quantitation of fluoride ion released sarin in red blood cell samples by gas chromatography-chemical ionization mass spectrometry using isotope dilution and large-volume injection.
Jakubowski EM, McGuire JM, Evans RA, Edwards JL, Hulet SW, Benton BJ, Forster JS, Burnett DC, Muse WT, Matson K, Crouse CL, Mioduszewski RJ, Thomson SA.
Research and Technology Directorate, U.S. Army ECBC, APG-EA, Edgewood, Maryland 21010, USA. edward.m.jakubowski@us.army.mil
A new method for measuring fluoride ion released isopropyl methylphosphonofluoridate (sarin, GB) in the red blood cell fraction was developed that utilizes an autoinjector, a large-volume injector port (LVI), positive ion ammonia chemical ionization detection in the SIM mode, and a deuterated stable isotope internal standard. This method was applied to red blood cell (RBC) and plasma ethyl acetate extracts from spiked human and animal whole blood samples and from whole blood of minipigs, guinea pigs, and rats exposed by whole-body sarin inhalation. Evidence of nerve agent exposure was detected in plasma and red blood cells at low levels of exposure. The linear method range of quantitation was 10-1000 pg on-column with a detection limit of
approximately 2-pg on-column. In the course of method development, several conditions were optimized for the LVI, including type of injector insert, injection volume, initial temperature, pressure, and flow rate. RBC fractions had advantages over the plasma with respect to assessing nerve agent exposure using the fluoride ion method especially in samples with low serum
butyrylcholinesterase activity.
Publication Types: Validation Studies
PMID: 15239856 [PubMed - indexed for MEDLINE]

51: J Anal Toxicol. 2004 Jul-Aug;28(5):352-6.
Analysis of the sulfur mustard metabolite 1,1'-sulfonylbis[2-S-(N-acetylcysteinyl)ethane] in urine by negative ion electrospray liquid chromatography- tandem mass spectrometry.
Read RW, Black RM.
Defence Science and Technology Laboratory, Porton Down, Salisbury, SP4 0JQ, United Kingdom.
A method is described for the analysis of the sulfur mustard metabolite 1,1'-sulfonylbis[2-S-(N-acetylcysteinyl)ethane] in human urine. The analyte was concentrated from urine on a polymeric SPE cartridge and analyzed by liquid chromatography-negative ion electrospray tandem mass spectrometry in the selected reaction monitoring mode. The limit of detection was 0.5-1 ng/mL. The metabolite was detected at concentrations close to the detection limit in samples of urine from two casualties accidentally exposed to sulfur mustard from a First World War munition.
PMID: 15239855 [PubMed - indexed for MEDLINE]

52: J Anal Toxicol. 2004 Jul-Aug;28(5):346-51.
Analysis of beta-lyase metabolites of sulfur mustard in urine by electrospray liquid chromatography-tandem mass spectrometry.
Read RW, Black RM.
Defence Science and Technology Laboratory, Porton Down, Salisbury, SP4 0JQ, United Kingdom.
A method is described for the analysis of b-lyase metabolites of sulfur mustard, 1-methylsulfinyl-2- [2-(methylthio)ethylsulfonyl]ethane and 1,1'-sulfonylbis [2-(methylsulfinyl)ethane], in human urine. The analytes were concentrated from urine on an ENV+ solid-phase extraction cartridge and analyzed by liquid chromatography-positive ion electrospray-tandem mass spectrometry in the selected reaction monitoring mode. Quantitation was performed against deuterated

internal standards. Limits of detection were 0.1-0.5 ng/mL. The metabolites were detected in samples of urine from human casualties of sulfur mustard poisoning. The method provides a simpler alternative to gas chromatography-tandem mass spectrometry analysis, avoiding the need for reduction to less polar analytes.
PMID: 15239854 [PubMed - indexed for MEDLINE]

53: J Anal Toxicol. 2004 Jul-Aug;28(5):339-45.
A rapid, sensitive method for the quantitation of specific metabolites of sulfur mustard in human urine using isotope-dilution gas chromatography-tandem mass spectrometry.
Young CL, Ash D, Driskell WJ, Boyer AE, Martinez RA, Silks LA, Barr JR.
Centers for Disease Control and Prevention, National Center for Environmental Health, 4770 Buford Highway NE, Mailstop F-47, Atlanta, Georgia 30341, USA.
Sulfur mustard agent (HD) (2,2'-dichloroethyl sulfide), a Schedule I compound on the Chemical Weapons Convention Schedule of Chemicals, remains a public health concern because it is simple to synthesize and it is in the chemical weapon stockpiles of several countries. A sensitive, rapid, accurate, and precise method was developed to quantitate trace levels of 1,1'-sulfonylbis
[2-(methylthio) ethane] (SBMTE) in human urine as a means of assessing exposure to HD. The method used immobilized liquid-liquid extraction with diatomaceous earth, followed by the analysis of the urine extract using isotope-dilution gas chromatography-tandem mass spectrometry. Relative standard deviations were less than 8.6% at 1 ng/mL and 3.6% at 20 ng/mL. The limit of detection for SBMTE was 0.038 ng/mL in 0.5 mL of urine.
Publication Types: Validation Studies
PMID: 15239853 [PubMed - indexed for MEDLINE]

54: J Anal Toxicol. 2004 Jul-Aug;28(5):333-8.
Retrospective detection of exposure to sulfur mustard: improvements on an assay for liquid chromatography-tandem mass spectrometry analysis of albumin-sulfur mustard adducts.
Noort D, Fidder A, Hulst AG, Woolfitt AR, Ash D, Barr JR.
Department of Chemical & Biological Protection, TNO Prins Maurits Laboratory, P.O. Box 45, 2280 AA Rijswijk, The Netherlands. noortd@pml.tno.nl
We here report on the further development of the method comprising the pronase digestion of albumin alkylated by sulfur mustard and the subsequent mass spectrometric analysis of an adducted tripeptide. This includes significant improvements in both the albumin isolation procedure and the automation of the microliquid chromatography-electrospray-tandem mass spectrometric analysis. We also report on the results of a small reference range study, in which we have established that there are no detectable interferences in sera from unexposed individuals.
PMID: 15239852 [PubMed - indexed for MEDLINE]

55: J Anal Toxicol. 2004 Jul-Aug;28(5):320-6.
Quantitation of biomarkers of exposure to nitrogen mustards in urine from rats dosed with nitrogen mustards and from an unexposed human population.
Lemire SW, Barr JR, Ashley DL, Olson CT, Hayes TL.
Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia 30341-3724, USA. SGL4@CDC.GOV
The nitrogen mustards bis(2-chloroethyl)ethylamine (HN1), bis(2-chloroethyl)methylamine (HN2), and tris(2-chloroethyl)amine (HN3) have the potential to be used as chemical terrorism agents because of their extreme vesicant properties. We modified a previously reported method to incorporate automated solid-phase extraction, improve chromatography, and include the
urinary metabolite for HN3. The improved method was used to measure levels of the urinary metabolites N-ethyldiethanolamine (EDEA), N-methyldiethanolamine (MDEA), and triethanolamine (TEA) in rats dosed with HN1, HN2, and HN3, respectively, and to establish background levels of EDEA, MDEA, and TEA in human urine samples from a population with no known exposure to nitrogen mustards. Rat dosing experiments confirmed that EDEA, MDEA, and TEA could be detected in urine for at least 48 h after exposure to HN1, HN2, and HN3, respectively. Substantial amounts of EDEA (89 ng/mL), MDEA (170 ng/mL), and TEA (1105

ng/mL) were measured in the urine of rats exposed to 10 mg HN1, HN2, and HN3, respectively, 48 h after exposure. The background concentrations for TEA in the human population ranged from below the limit of detection (LOD 3 ng/mL) to approximately 6500 ng/mL. Neither EDEA (LOD 0.4 ng/mL) nor MDEA (LOD 0.8 ng/mL) was detected above the LOD in the human samples.
PMID: 15239850 [PubMed - indexed for MEDLINE]

56: J Anal Toxicol. 2004 Jul-Aug;28(5):316-9.
Standard operating procedure for immunuslotblot assay for analysis of DNA/sulfur mustard adducts in human blood and skin.
van der Schans GP, Mars-Groenendijk R, de Jong LP, Benschop HP, Noort D.
TNO Prins Maurits Laboratory, P.O. Box 45, 2280 AA Rijswijk, The Netherlands.
A standard operating procedure has been developed for an immunoslotblot assay of sulfur mustard adducts to DNA in human blood and skin for use in a field laboratory. A minimum detectable level of exposure of human blood in vitro (> or = 50 nM) sulfur mustard is feasible with the assay. In the case of human skin, a 1 s exposure to saturated sulfur mustard vapor (830 mg/m(-3)) could still be detected.
PMID: 15239849 [PubMed - indexed for MEDLINE]

57: J Anal Toxicol. 2004 Jul-Aug;28(5):311-5.
Procedure for monitoring exposure to sulfur mustard based on modified edman degradation of globin.
Noort D, Fidder A, Benschop HP, De Jong LP, Smith JR.
TNO Prins Maurits Laboratory, P.O. Box 45, 2280 AA Rijswijk, The Netherlands.
noortd@pml.tno.nl
A procedure for the modified Edman degradation of globin for determination of sulfur mustard adducts to the N-terminal valine residue in human hemoglobin has been developed for use under field laboratory conditions. The minimum detectable exposure level of human blood (in vitro) to sulfur mustard using this procedure is 100 nM. The interindividual and intraindividual variabilities of the procedure were acceptable (standard deviation < 10% and < 20%, respectively). The procedure could be properly set up and carried out in another laboratory within one working day, demonstrating its robustness.
PMID: 15239848 [PubMed - indexed for MEDLINE]

58: J Anal Toxicol. 2004 Jul-Aug;28(5):306-10.
Monitoring sulfur mustard exposure by gas chromatography-mass spectrometry analysis of thiodiglycol cleaved from blood proteins. Capacio BR, Smith JR, DeLion MT, Anderson DR, Graham JS, Platoff GE, Korte WD.
U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland 21010-5400, USA.
A gas chromatography-mass spectrometry method for determining exposure to the chemical warfare agent 2,2'-dichlorodiethyl sulfide (sulfur mustard; HD) has been developed. The technique is based upon quantitating thiodiglycol (TDG) released from blood protein adducts that are formed upon exposure to HD. Protein was precipitated from plasma, whole blood, or packed red blood cells (RBCs) and then treated with sodium hydroxide to liberate protein-bound TDG. The TDG was derivatized with pentafluorobenzoyl chloride that enabled sensitive detection by
negative-ion chemical ionization. Octadeuterothiodiglycol was used as an internal standard. Exposure of human plasma to HD (25 nM to 400 nM) resulted in a linear relationship (r2 = 0.9995) between HD concentration and released TDG levels with means ranging from 2.0 to 38 pg/mg protein. The coefficients of variation expressed as a percentage for the data points ranged from 2 to 11.5%. The application of this procedure was demonstrated in two HD animal exposure
models. African green monkeys (Chlorocebus aethiops) were exposed intravenously to 1 mg/kg HD, and TDG levels in blood samples were analyzed out to 45 days post-exposure. Mean TDG levels were determined to be 220 pg/mg protein on day 1 and declined to 10 pg/mg protein on day 45. Yorkshire cross pigs (Sus scrofa) were cutaneously exposed to neat liquid HD, and TDG levels in plasma were determined out to 21 days following exposure. Mean

TDG levels were found to be 60 pg/mg protein on day one and decreased to an average of 4 pg/mg protein on
day 21. The data from this study indicate that the assay is sensitive and provide a relatively simple approach to assay TDG cleaved from blood proteins at relatively long time frames (21-45 days) after HD exposure. The utility of the method has been demonstrated in vivo in a non-human primate and pig HD exposure model.
PMID: 15239847 [PubMed - indexed for MEDLINE]

59: J Antimicrob Chemother. 2004 Dec;54(6):1134-8. Epub 2004 Oct 27.
Antibiotic susceptibility of 65 isolates of Burkholderia pseudomallei and Burkholderia mallei to 35 antimicrobial agents.
Thibault FM, Hernandez E, Vidal DR, Girardet M, Cavallo JD.
Centre de Recherches du Service de Sante des Armees Emile Parde, Departement de Biologie des Agents Transmissibles, F-38702 La Tronche, France. fthibault@crssa.net
OBJECTIVES: Fifty isolates of Burkholderia pseudomallei and 15 isolates of Burkholderia mallei were tested for their susceptibilities to 35 antimicrobial agents, including agents not previously tested against these bacteria. METHODS: MICs were determined by agar dilution in Mueller-Hinton medium. RESULTS: Among the antibiotics tested, lower MICs were obtained with imipenem, ceftazidime, piperacillin, piperacillin/tazobactam, doxycycline and minocycline. Fluoroquinolones and aminoglycosides had poor activities. A single clinical isolate of B. pseudomallei was resistant to ceftazidime, co-amoxiclav and doxycycline but remained susceptible to imipenem. CONCLUSIONS: Although B. mallei MICs are often lower, the overall results underline the importance of resistance in both species. The susceptibilities measured are consistent with the current recommendations for the treatment of B. pseudomallei and B. mallei infections.
PMID: 15509614 [PubMed - indexed for MEDLINE]

60: J Appl Toxicol. 2004 Nov-Dec;24(6):475-83.
Low levels of sarin affect the EEG in marmoset monkeys: a pilot study.
van Helden HP, Vanwersch RA, Kuijpers WC, Trap HC, Philippens IH, Benschop HP.
Department of Medical Countermeasures. TNO Prins Maurits Laboratory, PO Box 45, 2280 AA Rijswijk, The Netherlands. helden@pml.tno.nl
The main purpose of this pilot study was to estimate the lowest observable adverse effect level (LOAEL) for the electroencephalogram (EEG) upon long-term, low-level exposure of vehicle-pretreated and pyridostigmine-pretreated marmoset monkeys to sarin vapour. This is the C.t value (t=5 h) of exposure at which the EEG becomes significantly different from that resulting from air exposure of the same animals. The LOAELs for effects on the EEG in vehicle- and
pyridostigmine-pretreated marmosets appeared to be 0.2 and 0.1 mg min m(-3), respectively. Comparatively, the latter LOAEL values are at least an order of magnitude lower than the previously established LOAEL for miosis and only 2-5 times higher than the lowest observable effect level (LOEL) of bound sarin in blood.The second aim of the study was to analyse the EEG of the same marmosets again during a 5-h exposure to air 1 year after exposure to sarin vapour. All the marmosets still demonstrated significant ($P < 0.05$) EEG differences. In most vehicle-pretreated marmosets the energy (microV2) per EEG band was higher than that observed 1 year earlier, which might indicate that neurons had become more sensitive to excitation. This phenomenon was less pronounced in pyridostigmine-pretreated animals. Visual examination of the EEG records revealed clear bursts of alpha frequencies (ca. 9 Hz), resembling sleep-spindles, that were present more frequently in both groups of exposed marmosets than in naïve animals. These late changes in spindle oscillation might be the result of changes in the cholinergic system due to exposure to sarin vapour 1 year previously. In conclusion, EEG abnormalities persisting for more than 1 year may occur in humans during long-term (5 h) exposure to subclinical levels of sarin that are not detectable by the currently fielded alarm systems.
PMID: 15558834 [PubMed - indexed for MEDLINE]

61: J Appl Toxicol. 2004 Nov-Dec;24(6):493-5.
Delayed haematological complications of mustard gas.

Ghanei M.
Department of Internal Medicine, Baqiyatallah University of Medical Sciences, Chemical Injured Research Centre, Tehran, Iran. m.ghanei@bmsu.ac.ir
Haematopoiesis could be affected by mustard gas. We randomly selected 318 chemical victims exposed to mustard gas and compared their cell blood counts and peripheral blood smears (PBS) with those of 377 healthy men, and also various haematological indices of 57 of these victims compared with previous data 5 years ago.The average number of red blood cells and haemoglobin of victims compared with the controls was not significantly different, but they were increased compared with data from 5 years ago. White blood cell counts, neutrophils and lymphocytes did not show any clinically meaningful difference compared with the control group but 20 cases with atypical lymphocytes in their PBS have been found.Change in lymphocyte shape may be related to committed stem cell involvement. Further studies on bone marrow cells and cell markers are needed to document this hypothesis. The mild increase in erythroid cells and haemoglobin concentration may be due to chronic obstructive pulmonary disorder and other respiratory diseases in these patients.
PMID: 15558826 [PubMed - indexed for MEDLINE]

62: J Clin Invest. 2005 Feb;115(2):231-3.
Comment on: J Clin Invest. 2005 Feb;115(2):379-87.
Host-based antipoxvirus therapeutic strategies: turning the tables.
Fauci AS, Challberg MD.
National Institute of Allergy and Infectious Diseases, NIH, Bethesda, Maryland 20892-2520, USA. afauci@niaid.nih.gov
The potential threat of the smallpox virus as a bioterror weapon has long been recognized, and the need for developing suitable countermeasures has become especially acute following the events of September 2001. Traditional antiviral agents interfere with viral proteins or functions. In a new study, Yang et al. focus instead on host cellular pathways used by the virus. A drug that
interferes with the cellular ErbB-1 signal transduction pathway, activated by smallpox growth factor, sheds new light on how the virus replicates in the cell. Drugs that target the ErbB-signaling pathways represent a promising new class of antiviral agents.
Publication Types: Comment Review Review, Tutorial
PMID: 15690079 [PubMed - indexed for MEDLINE]

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Emergency preparedness: a new role for the dental practitioner.
Lopatin DE.
University of Michigan School of Dentistry, USA. lopatin@umich.edu
PMID: 15651160 [PubMed - indexed for MEDLINE]

64: J Pediatr. 2005 Jan;146(1):8-10.
Comment on: J Pediatr. 2005 Jan;146(1):41-4.
Safety of adult nerve agent autoinjectors in children.
Aaron C.
Publication Types: Comment Editorial
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65: J Vet Med Educ. 2004 Winter;31(4):391-400.
Food supply veterinary medicine: creating an awareness of livestock security risks.
Uhlenhopp E, Brown C, Ibarra P, Padilla EG, Rodezno LE, Slack G.
Outreach Academy for Veterinary Medicine and Rural Community Development, Iowa State University, 1802 Elwood Drive, Amies, IA 50011-1250, USA. uhlen@iastate.edu
PMID: 15551236 [PubMed - indexed for MEDLINE]

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Bioterrorism: EMS response to deadly infections.
Miller GT, Scott JA, Brotons AA, Frometa O, Gordon DL.

Division of Emergency Medicine, Center for Research in Medical Education, University of Miami School of Medicine, Miami, FL, USA.
PMID: 15662346 [PubMed - indexed for MEDLINE]

67: Lancet. 2005 Mar 2;365(9462):844.
Doctors and bioterrorism.
Rega PP.
Publication Types: Letter
PMID: 15752524 [PubMed - indexed for MEDLINE]

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Woodall JP.
Publication Types: Letter
PMID: 15721462 [PubMed - indexed for MEDLINE]

69: Med Confl Surviv. 2004 Oct-Dec;20(4):334-43.
Contamination and compensation: Gruinard as a 'menace to the mainland'.Willis EA.

Medact, London. e.a.willis@tinyworld.co.uk
The decades-long contamination of Gruinard Island by anthrax is now a well-known part of the history of biological weapons (BW) development, as well as that of military encroachments in the Scottish Highlands and Islands (and the authorities' rather less persistent efforts at damage limitation). Some accounts have included the related episode, reportedly well-remembered by local people, of anthrax contamination on the mainland close to Gruinard. This occurred in
1942--43, when BW experiments were conducted on the island as part of the war effort by scientists from Porton Down under the auspices of the British government. After much top-level discussion, payments were made to the owners of animals that had died as a result of the contamination. The episode had a bearing on discussions about the future of the island and on subsequent policy with regard to the siting, conduct and secrecy of BW experiments.
Publication Types: Historical Article
PMID: 15688884 [PubMed - indexed for MEDLINE]

70: Med Hypotheses. 2005;64(6):1248-9.
Therapy of newly emerging mutant viral disorders and role in bioterrorism.
Ambrus JL Sr, Ambrus JL Jr, Ambrus CM.
Department of Medicine, State University of New York at Buffalo, Buffalo General Hospital/Kaleida Health System, 100 High Street, Rm. E-320, Buffalo, NY 14203, USA. Tel.: +716 859 1399; fax: +716 859 3659.
Publication Types: Letter
PMID: 15823736 [PubMed - in process]

71: Mil Med. 2005 Jan;170(1):52-6.
N-acetyl-L-Cysteine as prophylaxis against sulfur mustard.
Bobb AJ, Arfsten DP, Jederberg WW.
Naval Health Research Center Detachment, Toxicology, 2729 R Street, Building 837, Area B, Wright Patterson AFB, OH 45433-7903, USA.
Sulfur mustard (HD) is a blister agent targeting the eyes, respiratory system, skin, and possibly other organs. Extensive exposure can destroy the immune system by destruction of bone marrow cells. There is no antidote for HD or effective treatment other than rapid decontamination. Clinical trials have demonstrated activity for N-acetyl-L-cysteine (NAC) against a number of significant human pathologies involving free radicals, and animal and tissue studies have suggested efficacy for NAC as a chemoprotectant against many toxic chemicals. Among these are studies demonstrating that NAC significantly reduces the effects of HD and HD simulants, both in cultured cells and animals. Given the historical effectiveness of HD, the lack of any effective treatment, the demonstrated chemoprotective properties of NAC, its low toxicity, the lack of

regulatory controls, and the data supporting efficacy against HD effects, we suggest daily oral administration of the maximum safe dose of NAC to personnel entering combat zones.
Publication Types: Review Review, Tutorial
PMID: 15724855 [PubMed - indexed for MEDLINE]

72: Mil Med. 2004 Nov;169(11):856-62.
Clinical aspects of percutaneous poisoning by the chemical warfare agent VX: effects of application site and decontamination.
Hamilton MG, Hill I, Conley J, Sawyer TW, Caneva DC, Lundy PM.
Medical Therapy Group, Chemical Biological Defence Section, Defence Research and Development Canada, Suffield, Box 4000, Medicine Hat, Alberta T1A 8K6, Canada.
O-ethyl S-(2-diisopropylaminoethyl) methylphosphonothioate (VX) is an extremely toxic organophosphate nerve agent that has been weaponized and stockpiled in a number of different countries, and it has been used in recent terrorist events. It differs from other well-known organophosphate nerve agents in that its primary use is as a contact poison rather than as an inhalation hazard. For this reason, we examined the effects of application site and skin decontamination on VX toxicity in anesthetized domestic swine after topical application. VX applied to the surface of the ear rapidly resulted in signs of toxicity consistent with the development of cholinergic crisis, including apnea and death. VX on the epigastrium resulted in a marked delayed development of toxic signs, reduced toxicity, and reduction in the rate of cholinesterase depression compared with animals exposed on the ear. Skin decontamination (15 minutes post-VX on the ear) arrested the development of clinical signs and prevented further cholinesterase inhibition and death. These results confirm earlier work that demonstrates the
importance of exposure site on the resultant toxicity of this agent and they also show that decontamination postexposure has the potential to be an integral and extremely important component of medical countermeasures against this agent.
PMID: 15605929 [PubMed - indexed for MEDLINE]

73: Mil Med. 2004 Nov;169(11):850-5.
A review of multi-threat medical countermeasures against chemical warfare and terrorism.
Cowan FM, Broomfield CA, Stojiljkovic MP, Smith WJ.
US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD 21010-5400, USA.
The Multi-Threat Medical Countermeasure (MTMC) hypothesis has been proposed with the aim of developing a single countermeasure drug with efficacy against different pathologies caused by multiple classes of chemical warfare agents. Although sites and mechanisms of action and the pathologies caused by different chemical insults vary, common biochemical signaling pathways, molecular mediators, and cellular processes provide targets for MTMC drugs. This article will review the MTMC hypothesis for blister and nerve agents and will expand the scope of the concept to include other chemicals as well as briefly consider biological agents. The article will also consider how common biochemical signaling pathways, molecular mediators, and cellular processes that contribute to clinical pathologies and syndromes may relate to the toxicity of threat
agents. Discovery of MTMC provides the opportunity for the integration of diverse researchers and clinicians, and for the exploitation of cutting-edge technologies and drug discovery. The broad-spectrum nature of MTMC can augment military and civil defense to combat chemical warfare and chemical terrorism.
Publication Types: Review Review, Tutorial
PMID: 15605928 [PubMed - indexed for MEDLINE]

74: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:179-83.
National symptom surveillance using calls to a telephone health advice service--United Kingdom, December 2001-February 2003.
Cooper DL, Smith G, Baker M, Chinemana F, Verlander N, Gerard E, Hollyoak V, Griffiths R.
Health Protection Agency West Midlands, Floor 2, Lincoln House, Heartlands Hospital, Birmingham, England B9 5SS. Duncan.Cooper@HPA.org.uk

INTRODUCTION: Recent terrorist activity has highlighted the need to improve surveillance systems for the early detection of chemical or biologic attacks. A new national surveillance system in the United Kingdom (UK) examines symptoms reported to NHS Direct, a telephone health advice service. OBJECTIVES: The aim of the surveillance system is to identify an increase in symptoms indicative of early stages of illness caused either by a deliberate release of a biologic or chemical agent or by common infections. METHODS: Data relating to 10 key syndromes (primarily respiratory and gastrointestinal) are received electronically from 23 call centers covering England and Wales. Data are analyzed daily and statistically significant excesses, termed exceedances, in calls are automatically highlighted and assessed by a multidisciplinary team. RESULTS: During December 2001-February 2003, a total of 1,811 exceedances occurred, of which 126 required further investigation and 16 resulted in alerts to local or national health-protection teams. Examples of these investigations are described. CONCLUSION: Surveillance of call-center data has detected substantial levels of specific syndromes at both national and regional levels. Although no deliberate release of a biologic or chemical agent has been detected thus far by this or any other surveillance system in the UK, the NHS Direct surveillance system continues to be refined.
PMID: 15717389 [PubMed - indexed for MEDLINE]

75: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:152-8.
Bio-ALIRT biosurveillance detection algorithm evaluation.
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Potomac Institute for Policy Studies, 901 N. Stuart Street, Suite 200, Arlington, Virginia 22203, USA. dsiegrist@potomacinstitute.org.
INTRODUCTION: Early detection of disease outbreaks by a medical biosurveillance system relies on two major components: 1) the contribution of early and reliable data sources and 2) the sensitivity, specificity, and timeliness of biosurveillance detection algorithms. This paper describes an effort to assess leading detection algorithms by arranging a common challenge problem and providing a common data set. OBJECTIVES: The objectives of this study were to determine whether automated detection algorithms can reliably and quickly identify the onset of natural disease outbreaks that are surrogates for possible terrorist pathogen releases, and do so at acceptable false-alert rates (e.g., once every 2-6 weeks). METHODS: Historic de-identified data were obtained from five metropolitan areas over 23 months; these data included International Classification of Diseases, Ninth Revision (ICD-9) codes related to respiratory
and gastrointestinal illness syndromes. An outbreak detection group identified and labeled two natural disease outbreaks in these data and provided them to analysts for training of detection algorithms. All outbreaks in the remaining test data were identified but not revealed to the detection groups until after their analyses. The algorithms established a probability of outbreak for each day's counts. The probability of outbreak was assessed as an "actual" alert for different false-alert rates. RESULTS: The best algorithms were able to detect all of the outbreaks at false-alert rates of one every 2-6 weeks. They were often able to detect for the same day human investigators had identified as the true start of the outbreak.
CONCLUSIONS: Because minimal data exists for an actual biologic attack, determining how quickly an algorithm might detect such
an attack is difficult. However, application of these algorithms in combination with other data-analysis methods to historic outbreak data indicates that biosurveillance techniques for analyzing syndrome counts can rapidly detect seasonal respiratory and gastrointestinal illness outbreaks. Further research is needed to assess the value of electronic data sources for predictive detection.
In addition, simulations need to be developed and implemented to better characterize the size and type of biologic attack that can be detected by current methods by challenging them under different projected operational conditions.
PMID: 15714645 [PubMed - indexed for MEDLINE]

76: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:74-8.
Scan statistics for temporal surveillance for biologic terrorism.
Wallenstein S, Naus J.

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INTRODUCTION: Intentional releases of biologic agents are often designed to maximize casualties before diagnostic detection. To provide earlier warning, syndromic surveillance requires statistical methods that are sensitive to an abrupt increase in syndromes or symptoms associated with such an attack. OBJECTIVES: This study compared two different statistical methods for detecting a relatively abrupt increase in incidence. The methods were based on the number of observations in a moving time window. METHODS: One class of surveillance
techniques generates a signal based on values of the generalized likelihood ratio test (GLRT). This surveillance method is relatively well-known and requires simulation, but it is flexible and, by construction, has the appropriate type I error. An alternative surveillance method generates a signal based on the p-values for the conventional scan statistic. This test does not require simulation, complicated formulas, or use of specialized software, but it is based on approximations and thus can overstate or understate the probability of interest. RESULTS: This study compared statistical methods by using brucellosis data collected by CDC. The methods provided qualitatively similar results. CONCLUSIONS: Relatively simple modification of existing software should be considered so that when GLRTs are performed, the appropriate function will be maximized. When a health department has data that indicate an unexpected increase in rates but its staff lack experience with existing software for surveillance based on GLRTs, alternative methods that only require computing Poisson probabilities can be used.
PMID: 15714633 [PubMed - indexed for MEDLINE]

77: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:67-73.
Role of data aggregation in biosurveillance detection strategies with applications from ESSENCE.
Burkom HS, Elbert Y, Feldman A, Lin J.
Johns Hopkins University Applied Physics Laboratory, 11100 Johns Hopkins Road, Mailstop 8-224, Laurel, MD 20723, USA. Howard.Burkom@jhuapl.edu
INTRODUCTION: Syndromic surveillance systems are used to monitor daily electronic data streams for anomalous counts of features of varying specificity. The monitored quantities might be counts of clinical diagnoses, sales of over-the-counter influenza remedies, school absenteeism among a given age group, and so forth. Basic data-aggregation decisions for these systems include determining which records to count and how to group them in space and time.
OBJECTIVES: This paper discusses the application of spatial and temporal data-aggregation strategies for multiple data streams to alerting algorithms appropriate to the surveillance region and public health threat of interest. Such a strategy was applied and evaluated for a complex, authentic, multisource, multiregion environment, including >2 years of data records from a
system-evaluation exercise for the Defense Advanced Research Project Agency (DARPA). METHODS: Multivariate and multiple univariate statistical process control methods were adapted and applied to the DARPA data collection. Comparative parametric analyses based on temporal aggregation were used to optimize the performance of these algorithms for timely detection of a set of outbreaks identified in the data by a team of epidemiologists. RESULTS: The sensitivity and timeliness of the most promising detection methods were tested at empirically calculated thresholds corresponding to multiple practical false-alert rates. Even at the strictest false-alert rate, all but one of the outbreaks were detected by the best method, and the best methods achieved a 1-day median time before alert over the set of test outbreaks. CONCLUSIONS:
These results indicate that a biosurveillance system can provide a substantial alerting-timeliness advantage over traditional public health monitoring for certain outbreaks. Comparative analyses of individual algorithm results indicate further achievable improvement in sensitivity and specificity.
PMID: 15714632 [PubMed - indexed for MEDLINE]

78: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:56-8.
Syndromic surveillance at hospital emergency departments--southeastern Virginia.

Yuan CM, Love S, Wilson M.
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Hospital emergency department (ED) syndromic surveillance has been proposed for early detection of a large-scale biologic terrorist attack. However, questions remain regarding its usefulness. The authors examined the use of active syndromic surveillance at hospital EDs in Virginia for early detection of disease events and analyzed the effectiveness of the cumulative sum (CUSUM) algorithm in identifying disease events from syndromic data. Daily chief-complaint data were collected for 10 months at seven hospital EDs in southeastern Virginia. Data were categorized into seven syndromes (fever, respiratory distress, vomiting, diarrhea, rash, disorientation, and sepsis), and the CUSUM algorithm was used to detect anomalies in each of the seven syndromes at each hospital. Fever and respiratory distress syndromes exhibited monthly and ambient-temperature-specific trends consistent with southeastern Virginia's influenza season. Furthermore, preliminary frequencies of hospital ED patient chief complaints in southeastern Virginia during a 10-month period were produced by using syndromic data. This system represents an example of a local syndromic surveillance program serving multiple cities in a limited geographic region.
PMID: 15714630 [PubMed - indexed for MEDLINE]

79: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:53-5.
BioSense--a national initiative for early detection and quantification of public health emergencies.
Loonsk JW.
Information Resources Management Office, CDC, 1600 Clifton Rd, Mailstop D-45, Atlanta, GA 30333, USA. jloonsk@cdc.gov
BioSense is a national initiative to enhance the nation's capability to rapidly detect, quantify, and localize public health emergencies, particularly biologic terrorism, by accessing and analyzing diagnostic and prediagnostic health data. BioSense will establish near real-time electronic transmission of data to local, state, and federal public health agencies from national, regional, and local health data sources (e.g., clinical laboratories, hospital systems, ambulatory care sites, health plans, U.S. Department of Defense and Veterans Administration medical treatment facilities, and pharmacy chains).
PMID: 15714629 [PubMed - indexed for MEDLINE]

80: MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53 Suppl:43-9.
National Bioterrorism Syndromic Surveillance Demonstration Program.
Yih WK, Caldwell B, Harmon R, Kleinman K, Lazarus R, Nelson A, Nordin J, Rehm B, Richter B, Ritzwoller D, Sherwood E, Platt R.
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The National Bioterrorism Syndromic Surveillance Demonstration Program identifies new cases of illness from electronic ambulatory patient records. Its goals are to use data from health plans and practice groups to detect localized outbreaks and to facilitate rapid public health follow-up. Data are extracted nightly on patient encounters occurring during the previous 24 hours. Visits or
calls with diagnostic codes corresponding to syndromes of interest are counted; repeat encounters are excluded. Daily counts of syndromes by zip code are sent to a central data repository, where they are statistically analyzed for unusual clustering by using a model-adjusted SaTScan approach. The results and raw data are displayed on a restricted website. Patient-level information stays at the originating health-care organization unless required by public health authorities. If a cluster surpasses a threshold of statistical aberration chosen by the corresponding public health department, an electronic alert can be sent to that department. The health department might then call a clinical responder, who has electronic access to records of cases contributing to clusters. The system is flexible, allowing for changes in participating organizations, syndrome definitions, and alert thresholds. It is transparent to clinicians and

has been accepted by the health-care organizations that provide the data. The system's data are usable by local and national health agencies. Its software is compatible with commonly used systems and software and is mostly open-source. Ongoing activities include evaluating the system's ability to detect naturally occurring outbreaks and simulated terrorism events, automating and testing alerts and response capability, and evaluating alternative data sources.
PMID: 15714626 [PubMed - indexed for MEDLINE]

81: Nat Biotechnol. 2004 Dec;22(12):1503-5.
Comment in: Nat Biotechnol. 2005 Feb;23(2):170.
US food safety under siege?
Gilmore R.
GIC Group, 1434 Duke Street, Alexandria, VA 22314, USA. rickgilmore@gicgroup.com
PMID: 15583650 [PubMed - indexed for MEDLINE]

82: Nat Biotechnol. 2004 Jun;22(6):656.
ELSI and bioterrorism countermeasures?
Green SK.
Publication Types: Letter
PMID: 15175678 [PubMed - indexed for MEDLINE]

83: Nat Med. 2004 Dec;10(12 Suppl):S130-6.
Advances in detecting and responding to threats from bioterrorism and emerging infectious disease.
Rotz LD, Hughes JM.
National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. lrotz@cdc.gov
Much progress has been made in recent years to strengthen local, state, national and international capacities to detect and respond to bioterrorism events and naturally occurring outbreaks of disease. New tools and systems are available to estimate the potential impact of a biological event and predict resource needs for effective response, enable earlier detection of an attack or outbreak, enhance diagnostic capacity and facilitate rapid intervention to mitigate the
impact of an event on a community. These advances have required new approaches to preparedness, planning and surveillance, as well as new partnerships and collaborations across a range of disciplines. We examine some of these developments, discuss potential uses and limitations of these approaches, and identify priorities for the future.
PMID: 15577931 [PubMed - indexed for MEDLINE]

84: Occup Health Saf. 2004 Dec;73(12):22, 24, 26.
Our emerging reliance on pervasive sensing.
Durstenfeld B.
RAE Systems Inc., Sunnyvale, CA, USA. bdurstenfeld@raesystems.com
PMID: 15638284 [PubMed - indexed for MEDLINE]

85: Pac Symp Biocomput. 2005;:248-59.
Identification of genomic signatures for the design of assays for the detection and monitoring of anthrax threats.
Draghici S, Khatri P, Liu Y, Chase KJ, Bode EA, Kulesh DA, Wasieloski LP, Norwood DA, Reifman J.
Dept of Computer Science, Wayne State University, Detroit, MI 48202, USA.
Sequences that are present in a given species or strain while absent from or different in any other organisms can be used to distinguish the target organism from other related or un-related species. Such DNA signatures are particularly important for the identification of genetic source of drug resistance of a strain or for the detection of organisms that can be used as biological agents
in warfare or terrorism. Most approaches used to find DNA signatures are laboratory based, require a great deal of effort and can only distinguish between two organisms at a time. We

propose a more efficient and cost-effective bioinformatics approach that allows identification of genomic fingerprints for a target organism. We validated our approach using a custom microarray, using sequences identified as DNA fingerprints of Bacillus anthracis. Hybridization results showed that the sequences found using our algorithm were truly unique to B. anthracis and were able to distinguish B. anthracis from its close relatives B. cereus and B. thuringiensis.
PMID: 15759631 [PubMed - indexed for MEDLINE]

86: PDA J Pharm Sci Technol. 2004 Nov-Dec;58(6):279-83.
Applying rapid microbiology techniques in the war against bioterrorism.
Costello C, Moldenhauer J.
Vectech Pharmaceutical Consultants, Inc.
Publication Types: Review Review, Tutorial
PMID: 15663058 [PubMed - indexed for MEDLINE]

87: Physician Exec. 2005 Jan-Feb;31(1):30-3.
Anthrax attacks, hurricanes and flu shot shortage test Agwunobi's skills.
Davis T.
PMID: 15732813 [PubMed - indexed for MEDLINE]

88: Prehospital Disaster Med. 2005 Jan-Feb;20(1):3-6.
Demystifying bioterrorism: misinformation and misperceptions.
Noji E, Goodwin T, Hopmeier M.
The true threat of bioterrorism remains mysterious and elusive to the common citizen. It principally has become the dominion of a few "experts", many of whom have limited apparent expertise, who have failed to effectively communicate the risks and realities to society, and have instead created an air of uncertainty surrounding the topic. Unlike the great classic deceptions of modern life (e.g., "the check is in the mail"), the misinformation and misperceptions associated
with bioterrorism can be dangerous and are not merely humorous. Indeed, it is possible to grasp the facts as well as fallacies associated with bioterrorism, and, as a result, demystify this nightmare scenario and prepare for the "unthinkable".
Publication Types: Editorial
PMID: 15748008 [PubMed - in process]

89: Protein Sci. 2004 Oct;13(10):2736-43. Epub 2004 Aug 31.
Improved stability of a protein vaccine through elimination of a partially unfolded state.
McHugh CA, Tammariello RF, Millard CB, Carra JH.
United States Army Medical Research Institute of Infectious Diseases, Department of Cell Biology and Biochemistry, 1425 Porter Street, Frederick, MD 21702, USA.
Ricin is a potent toxin presenting a threat as a biological weapon. The holotoxin consists of two disulfide-linked polypeptides: an enzymatically active A chain (RTA) and a galactose/N-acetylgalactosamine-binding B chain. Efforts to develop an inactivated version of the A chain as a vaccine have been hampered by limitations of stability and solubility. Previously, recombinant truncated versions of the 267-amino-acid A chain consisting of residues 1-33/44-198 or 1-198 were designed by protein engineering to overcome these limits and were shown to be effective and nontoxic as vaccines in mice. Herein we used CD, dynamic light scattering, fluorescence, and Fourier-transform infrared spectroscopy to examine the biophysical properties of these proteins. Although others have found that recombinant RTA (rRTA) adopts a partially unfolded,
molten globule-like state at 45 degrees C, rRTA 1-33/44-198 and 1-198 are significantly more thermostable, remaining completely folded at temperatures up to 53 degrees C and 51 degrees C, respectively. Deleting both an exposed loop region (amino acids 34-43) and the C-terminal domain (199-267) contributed to increased thermostability. We found that chemically induced denaturation of rRTA, but not the truncated variants, proceeds through at least a three-state
mechanism. The intermediate state in rRTA unfolding has a hydrophobic core accessible to ANS and an unfolded C-terminal domain. Removing the C-terminal domain changed the

mechanism of rRTA unfolding, eliminating a tendency to adopt a partially unfolded state. Our results support the conclusion that these derivatives are superior candidates for development as vaccines against ricin and suggest an approach of reduction to minimum essential domains for design of more thermostable recombinant antigens.
PMID: 15340172 [PubMed - indexed for MEDLINE]

90: Public Health Rep. 2005 Jan-Feb;120(1):11-8.
A model curriculum for public health bioterrorism education.
Dembek Z, Iton A, Hansen H.
Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington, CT 06030, USA. epibiochem@msn.com
Beginning with the spring semester of 2001, a course designed to prepare future public health leaders for potential bioterrorism events has been offered by the University of Connecticut Graduate Program in Public Health. Entitled "The Public Health Response to Bioterrorism," this popular course was one of the few developed by academic programs in the United States prior to the attack of September 11, 2001. The course utilizes innovative teaching methods and presentations by distinguished guest speakers to educate public health personnel, public health and medical students, and physicians and nurses about the complex issues involved in the public health response to bioterrorism. The instructional methods and curriculum can serve as prototypes for similar efforts.
PMID: 15736326 [PubMed - indexed for MEDLINE]

91: Science. 2005 Mar 25;307(5717):1881-2.
Ethics: a weapon to counter bioterrorism.
Somerville MA, Atlas RM.
McGill Centre for Medicine, Ethics, and Law, McGill University, Montreal, Canada, H3A 1W9.
PMID: 15790831 [PubMed - indexed for MEDLINE]

92: Science. 2005 Jan 28;307(5709):501.
Biodefense labs. Boston University Under Fire for Pathogen Mishap.
Lawler A.
Publication Types: News
PMID: 15681355 [PubMed - indexed for MEDLINE]

93: South Med J. 2005 Feb;98(2):259.
Is Japan sufficiently prepared to deal with bioterrorism?
Yokota T, Kojima S, Kikuchi S, Yamauchi H.
Publication Types: Letter
PMID: 15759967 [PubMed - in process]

94: Toxicol In Vitro. 2004 Oct;18(5):593-9.
An inhibitor of p38 MAP kinase downregulates cytokine release induced by sulfur mustard exposure in human epidermal keratinocytes.
Dillman JF 3rd, McGary KL, Schlager JJ.
Applied Pharmacology Branch, US Army Medical Research Institute of Chemical Defense, 3100 Ricketts Point Road, MCMR-U, Aberdeen Proving Ground, MD 21010-5400, USA. james.dillman@apg.amedd.army.mil
Sulfur mustard (2,2'-dichlorodiethyl sulfide, SM) is a potent alkylating agent that induces skin vessication after cutaneous exposure. Previous work has revealed that SM induces the production of inflammatory cytokines, including IL-8, IL-6, TNF-alpha, and IL-1beta, in keratinocytes. The p38 MAP kinase (MAPK14) signaling pathway is activated via phosphorylation in response to cellular stress and has been implicated in the upregulation of cytokines in
response to stress. We investigated the role of p38 MAP kinase in inflammatory cytokine upregulation following SM exposure. A dose response study in cultured human epidermal keratinocytes (HEK) revealed increasing phosphorylation of p38 MAP kinase in response to increasing concentrations of SM. A time course at the 200 microM exposure revealed that p38 MAP kinase phosphorylation is induced by 15 min post-exposure, peaks at 30 min and is

sustained at peak levels until 8 h post-exposure. Phosphorylation of the upstream kinase MKK3/6 was also detected. Assay of the SM-exposed HEK culture media for cytokines revealed that exposure to 200 microM SM increased IL-8, IL-6, TNF-alpha, and IL-1beta. When cells exposed to 200 microM SM were treated with the p38 MAP kinase inhibitor SB203580, the levels of IL-8, IL-6, and TNF-alpha and IL-1beta were significantly decreased when compared with cells that were untreated. These results show that p38 MAP kinase plays a role in SM-induced cytokine production in HEK and suggest that inhibiting this pathway may alleviate the profound inflammatory response elicited by cutaneous SM exposure.
PMID: 15251176 [PubMed - indexed for MEDLINE]

95: Transfusion. 2005 Mar;45(3):399-403.
Comment in: Transfusion. 2005 Mar;45(3):290-2.
Nucleic acid test screening of blood donors for orthopoxviruses can potentially prevent dispersion of viral agents in case of bioterrorism.
Schmidt M, Roth WK, Meyer H, Seifried E, Hourfar MK.
Institute of Transfusion Medicine and Immunohematology, German Red Cross, Johann Wolfgang Goethe University, Frankfurt, Germany. mschmidt@bsdhessen.de
BACKGROUND: Microbiologic agents such as variola virus (VAR) are very attractive for terrorism. As a result of international collaboration under the WHO eradication campaign, smallpox was declared eradicated in 1980. Therefore, the immunization programs were discontinued worldwide. Because most people are now immunologically naive, VAR is considered to be a potential threat agent or bioterrorist weapon. Real-time polymerase chain reaction (PCR) followed by melting analysis was developed for fast and safe analysis and allows differentiation of VAR from other orthopoxviruses (OPVs) like vaccinia or camelpox virus. STUDY DESIGN AND METHODS: A RealArt Orthopox LC PCR kit (Artus GmbH) was used to amplify OPV sequences from blood donor samples. A total of 31,500 blood donor samples were tested in minipools of up to 96 samples. To evaluate the sensitivity of the assay, routine donor minipools (90 +/- 6 samples
per pool) were spiked with vaccinia virus used as positive control. RESULTS: Specificity was 100 percent because none of 31,500 blood donors was positive for the presence OPV. The detection limit of the assay was 10.6 copies per PCR procedure. Therefore, a sensitivity of 1590 copies per mL was calculated. Overall, 0.28 percent of test results had to be considered invalid owing to
negative internal controls. CONCLUSION: The RealArt Orthopox LC PCR kit enables reliable detection of OPV DNA in viremic blood donor samples, even at the beginning of the disease when patients present minor clinical symptoms, and could be implemented in our routine screening procedure immediately. Thus, the assay could potentially help to prevent dispersion of viral agents by blood transfusion in case of bioterrorism.
PMID: 15752158 [PubMed - indexed for MEDLINE]

96: Transfusion. 2005 Mar;45(3):290-2.
Comment on: Transfusion. 2005 Mar;45(3):399-403.
Blood donor screening for agents of bioterror: more questions than answers.
Katz LM, Sayers M.
Publication Types: Comment Editorial
PMID: 15752144 [PubMed - indexed for MEDLINE]

97: US News World Rep. 2005 Mar 14;138(9):66.
Bioterrorism. It was unbelievable.
Spake A.
Publication Types: News
PMID: 15782813 [PubMed - in process]